Research (NAVIGATOR) trial, the short-acting sulphonylurea analogue, nateglinide failed to reduce overt type 2 diabetes and its complications, such as MI and stroke, in individuals with IGT. The ORIGIN Study did not demonstrate a reduction of CV events in IGT or newly-diagnosed diabetes with insulin glargine.

The concept of a metabolic memory supports the view, that earliest optimization of glucose control is essential for a long-term CV benefit in diabetes. This is also emphasized by the Joint Guidelines by the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD) on Diabetes, Prediabetes and Cardiovascular Disease.

Increasing the awareness for the association of IGT and increased CV risk together with the initiation of earliest preventive strategies is fundamental for a future reduction of CV events in diabetes.

ISP20: Should we still revascularize diabetic patients with coronary artery disease and how?

O. Varenne, Hôpital Cochin, Paris, France

Type 2 diabetes mellitus (DM2), expected to reach 4.4% of the world population in 2030, represents a major risk factor for coronary artery disease. Until recent years, coronary bypass grafting was the favoured choice for revascularization in multivessel patients with DM2. Percutaneous coronary intervention (PCI) and use of drug eluting stents (DES) have profoundly modified the therapeutic strategies but major adverse cardiac events remain more frequent in DM2 patients with CAD. In diabetic patients with selected lesions, the use of DES leads to a reduction of revascularizations compared to bare metal stents both with the sirolimus eluting stent (SES, CyphérÔ, Cordis, Johnson and Johnson) and with the paclitaxel eluting stent (PES, TaxusÔ, Boston Scientific). Compared to DES, surgical revascularization is associated with better outcomes in patients with moderate or severe coronary disease evaluated by the SYNTAX score. Last generation everolimus DES (EES, XienceÔ, Abbott vascular) have improved biomechanical properties associated with low rates of restenosis and stent thrombosis. They have recently been evaluated in diabetics-dedicated registry (FEDIX/MEDIX) with good clinical results at one year.

PCI is only one part of the treatment of diabetic patients with CAD. Improvement in the efficacy and the safety of new DES should be evaluated together with optimal medical therapy of DM2 and associated risk factors.

New generation DES may alter current recommendations for myocardial revascularization in diabetic patients.

ISP21: Which antiaggregant strategy in diabetic patients with coronary artery disease?

M. Gilard, Brest, France

Cardiovascular disease is the leading cause of morbidity and mortality in patients with diabetes. The concomitant presence of multiple classical cardiovascular risk factors in diabetic subjects contributes to enhanced atherothrombotic risk [1].

However, other risk factors may be important such as abnormal platelet function. Patients with diabetes mellitus (DM) are characterized by enhanced platelet reactivity and a reduced response to oral antiplatelet medications used for the prevention of ischaemic events. Clopidogrel non responsiveness is more prevalent in diabetic compared with nondiabetic patients and is highest among patients requiring insulin therapy [2-4]. There is a need for alternative platelet inhibition strategies.

The standard-dose prasugrel resulted in greater platelet inhibition in aspirin-treated patients with type 2 DM and coronary artery disease than double-dose clopidogrel. Prasugrel also resulted in a better response profile with lower rates of poor responders [5]. The efficacy of Ticagrelor (reversible oral P2Y12 receptor antagonist) is better than clopidogrel and reduced ischaemic events in acute coronary syndrome patients irrespective of diabetic status and glycaemic control, without an increase in major bleeding events [6].

The diabetic patient can benefit of revascularisation procedures, even if he is exposed to a higher incidence of complications after a coronary artery bypass graft or a percutaneous transluminal coronary angioplasty. The use of drug-eluting stents dramatically reduces the risk of restenosis as compared to bare-metal stents; nevertheless, the rate of restenosis remains almost double in diabetic patients compared to that observed in non-diabetic subjects. Efficacious antiplatelet therapy in the long run is mandatory in all diabetic patients treated with drug-eluting stents.

References:


ISP22: Metabolic determinants of cerebrovascular disease in type 2 diabetes

N. Lalic, University of Belgrade Faculty of Medicine, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia, Belgrade, Serbia

Epidemiological studies have postulated that prevalence of ischemic brain disease as well as the risk for ischemic stroke are significantly higher in patients with diabetes than in nondiabetics. However, the mechanisms underlying these influences are not yet elucidated.

Numerous studies have shown that insulin resistance (IR) can exert its influence on the development of atherosclerosis through different mechanisms, either directly, by inducing endothelial dysfunction, or indirectly, favoring risk factors for atherosclerosis such as hyperinsulinemia, hyperglycemia, dyslipidemia, hypertension, and hypofibrinolysis, which indicates a very complex relationship of IR and atherosclerosis.

When central nervous system is concerned, it has been shown that IR might be involved in different diseases, including cerebrovascular but also in neurodegenerative disorders and especially in different types of cognitive impairments.

The studies of metabolic determinants of cerebrovascular diseases, including ours, have shown that IR might play an important role in the occurrence of ischemic stroke, both in patients with type 2 diabetes (T2D) and in nondiabetics. In this context, our results demonstrated significantly decreased insulin sensitivity, evaluated using the minimal
model, in T2D with ischemic stroke in comparison to T2D patients without stroke. The lower insulin sensitivity, i.e. the increased IR, in the T2D patients was accompanied with increases in traditional risk factors, especially LDL-cholesterol levels, and the decreases in glutathione-dependent antioxidant enzyme activity. Those differences in metabolic risk factors could not be demonstrated among the subtypes of ischemic stroke in the T2D patients.

Although IR has been shown to play an important role in a range of neurodegenerative disorders (Huntington and Alzheimers disease, spinocerebellar ataxia), the accompanying pattern of metabolic changes is reported to be different. The differences are most prominent in the changes in lipid metabolism and in addition the IR in neurodegenerative diseases is shown to be accompanied with the decrease in insulin secretion even in nondiabetic subjects, which could not be demonstrated in cerebrovascular disorders in nondiabetics.

Due to the fact that both neurogenic and cerebrovascular components might contribute to cognitive dysfunction, which is reported to be frequent in diabetic patients, and with respect to the recent findings that insulin administration might improve cognitive function, the importance of the previously reported metabolic determinants for the development of cognitive dysfunction in T2D still remains to be clarified.

**ISP23: Aspirin efficacy in diabetes**

J.G. Dillinger1, C. Bal dit Sollier2, P. Henry1, L. Drouet2
1 Cardiology Department; 2 Angio-hematology Department and IVS, Lariboisière hospital, Paris 7 University, Paris, France

Diabetes is a major risk factor of cardiovascular morbidity and mortality. In such a pathology associated with a high incidence of cardiovascular events it should be easy to show the efficacy of an efficient therapy. But at the opposite every individual prospective and retrospective study (older studies as well as the most recent ones) evaluating the efficacy of aspirin failed to report a benefit in diabetic patients in cardiovascular disease. Several recent meta-analyses confirm and amplify the observation that diabetic patients don’t significantly benefit of an aspirin treatment in primary as well as in secondary prevention. The « AntiPlatelet Trialist’ Collaboration meta-analysis » showed in secondary prevention a limited relative benefit of an antiplatelet treatment (lower that what is observed in non diabetic patients) which is non significant when selecting the trials studying only aspirin as antiplatelet therapy. As a consequence diabetic patients can be considered resistant to the anti-thrombo-ischemic effects of aspirin. We were one of the first to demonstrate that among the causes of resistance to aspirin diabetic patients are characterized by a higher platelet turn over which explains the progressive loss of antiplatelet effect of aspirin after a delay dosing with a recovery of subnormal platelet functions before the next dosing in 20 to 30 % of diabetic patients. Several major groups have achieved consistent observations. The accelerated turn over of platelets in diabetic patients has several explanations. The possibilities to counteract this resistance are the improvement of the metabolic equilibrium of diabetics, the twice a day administration of aspirin or the switch to another antiplatelet agent. Among the other antiplatelet agents tested the first one was clopidogrel : even if the diabetics get a better clinical benefit with clopidogrel compared to aspirin (tested only in secondary prevention) the reduction of cardiovascular events is much less in diabetic patients than in non diabetic. This relative resistance of diabetic patients to clopidogrel is only partially explained by the accelerated platelet turn over but mostly explained differences in the metabolism of clopidogrel (a prodrug) in diabetic patients. Better understanding of the antiplatelet agents in diabetic patients should help to launch studies specifically designed for diabetic patients.

**ISP24: New oral anticoagulants**

S. Apostolakis MD, PhD, University of Birmingham Centre for Cardiovascular Sciences, United Kingdom

For more than 50 years vitamin K antagonists (VKAs) were the only orally available drugs for the prevention of thromboembolism in patients with atrial fibrillation (AF). Recently, a direct thrombin inhibitor (dabigatran) and two factor Xa inhibitors (apixaban and rivaroxaban) were approved for the same indication. New drugs have unique safety and efficacy profiles and they are expected to completely alter AF management. The new oral anticoagulants (OACs) differ significantly offering the clinician the chance to tailor anticoagulation to individual patient’s needs. Diabetic patients are a population of particular concern. Diabetic patients with AF are by definition at moderate-high risk for thromboembolism and should be treated with OAC. Patients with diabetes were adequately represented in landmark clinical trials that assessed safety and efficacy of new OACs. In the subgroup analyses, new OACs seemed to be at least as safe and effective as warfarin in diabetic patients.

Nevertheless, new OACs need to be handled with caution. Health care systems should emphasize on the implementations of the directions derived from their clinical trials. Physicians that handle these drugs should be aware of their limitations and contraindications. Moreover, new OACs might not require monitoring of their anticoagulation effects but the patient requires regular follow-up and reassessment of his thromboembolic and haemorrhagic risk. From that perspective new OACs should be ideally handled by specialized physicians preferably in the same organized infrastructures that handled VKAs. Organized anticoagulation clinics would provide guidance on who to treat and how intensively to treat and also provide immediate solutions in cases that anticoagulation should be ceased or even reversed. There are also instances where quantifying the anticoagulant effect may be important. The new drugs will be efficient, safe and cost-effective only if they are appropriately used.

**ISP25: Early left ventricular dysfunction in diabetes**

C. B. Giorda, Italy

T2DM is cause of CV complications, atherosclerosis, heart failure and death. DYDA is a prospective, multicenter epidemiological study in 960 T2DM patients, aged >45 years and without overt cardiac diseases. Baseline echocardiographic examination revealed a high prevalence of preclinical LV systolic (21%) and diastolic dysfunction (27%) or both (12%) (LVD), measured by midwall shortening (MFS) and transmital flow pattern, respectively, as previously reported. Patients were followed-up for 2 years. In the present abstract, we report data on echocardiographic re-evaluation and clinical events. Systolic LVD (SLVD) was defined as EF <50% or MFS <15%; diastolic LVD (DLVD) was identified in all conditions different from “normal”, defined as transmirtal E/A ratio between 0.75 and 1.5 and E velocity deceleration time >140 msec. The primary outcome was a composite of major events (all-cause death and hospital admissions). Secondary end-point was the incidence of new LVD.

Follow-up data were available on 957 patients. During the follow-up 15 deaths (1.6%, 3 CV death, 11 non CV death, 1 of unknown etiology) and 181 hospital admissions were observed in 139 patients (48 for CV cause, 133 for non CV cause). In multivariate analysis, older age (67 vs 56 yrs OR 1.41.95%CI 1.05-1.88), high LDL (134 vs 93 mg/dL OR 1.39, CI 1.08-1.78), low HDL (57 vs 42.5 mg/dL OR 1.39, CI 1.08-1.78), high HbA1c (7.6 vs 6.0% OR 1.3, CI 1.05-1.62), peripheral arterial disease (OR 3.49, CI 1.54-7.9) and treatment with